Regulatory news

Pre-market assessment

EMA publishes clinical reports

European Union – The EMA has started to give open access to clinical reports for new medicines for human use authorized in the EU on a new website, following the adoption of a new policy after extensive consultation with stakeholders. The website will include the clinical reports contained in applications for marketing authorization submitted to the Agency on or after 1 January 2015, and in applications for extension or modification of an indication, or for line extension, submitted on or after 1 July 2015. The data is intended to increase transparency, facilitate independent re-analysis and support efficient medicine development.

Data for two medicines were published initially, comprising over 100 clinical reports. EMA expects to offer access to approximately 4500 clinical reports per year. (1)

Data for two additional medicines followed one month later. (2)

Health Action International (HAI) has welcomed the move and has emphasized its strong support for the principle that clinical trial data must be made publicly available to all. (3)

► (1) EMA Press release, 20 October 2016.
(2) EMA Press release, 24 November 2016.

(3) HAI. Clinical Trial Data Transparency on Trial – EMA Under Pressure From Pharma Lawsuit. 1 December 2016.

Post-market surveillance

Social media campaign on reporting of medicines side effects

United Kingdom, European Union – On 7–11 November 2016 the MHRA held a social media campaign to promote reporting of suspected side effects as part of an EU-wide awareness week. Twenty-two EU Member States took part in the combined cross-European social media campaign organized under the Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action project, which aims to raise awareness of national reporting systems for suspected side effects in medicines.


EU project to strengthen market surveillance for medical devices

Bratislava, Slovakia – At the 39th meeting of the EU Competent Authorities for Medical Devices (CAMD) held in Bratislava in October 2016, the MHRA launched the Joint Action on Market Surveillance of Medical Devices. Post-marketing surveillance is a crucial part of health product regulation to make sure that medical devices are acceptably safe and perform as intended. The project aims to improve the coordination of surveillance activities by EU member states and to ensure adequate communications and cooperation.

EU–U.S. collaboration on medicines for rare diseases

European Union, United States of America – The EMA and the FDA have set up a new working group to share experiences and best regulatory practices in the development of medicines for rare diseases. Global collaboration in this area is particularly important to ensure that the few studies that can be conducted in the small patient populations can benefit all patients. The agencies will exchange information on topics such as the design of clinical trials and the use of statistical analysis methods, the selection and validation of trial endpoints, preclinical evidence to support development programmes, the design of post-marketing studies, and risk management strategies for long-term safety issues.

The existing EMA/FDA “Cluster on orphan medicinal products” will continue to focus on orphan designation and exclusivity.

► EMA News, 26 September 2016.

Mapping of global medicines regulatory initiatives

European Union – The EMA has published a comprehensive overview of global initiatives on medicine regulation. The mapping was carried out by EMA on behalf of the International Coalition of Medicines Regulatory Authorities (ICMRA). The aim of the mapping exercise was to raise awareness of ongoing activities, provide a basis for strategic coordination and identify possible gaps.

The report was presented at the 11th Summit of Heads of Medicines Regulatory Agencies and the annual ICMRA meeting held in Interlaken, Switzerland, on 11-13 October 2016. It includes wide-ranging activities such as the harmonization work of the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), and identifies areas of particular strategic interest for ICMRA including generic medicines, good manufacturing practice inspections, exchange of confidential information, supply-chain integrity, crisis management, pharmacovigilance and information technology systems.


EMA. Connecting the dots. Towards global knowledge of the international medicine regulatory landscape: mapping of international initiatives. 2016.
MHRA and Swissmedic sign agreement

Interlaken, Switzerland – The MHRA and Swissmedic have signed a Memorandum of Understanding (MoU). The agreement was signed on the sidelines of the 11th Summit of the Heads of Medicines Regulatory Agencies in Interlaken, Switzerland. It focuses on implementing a shared approach to complex challenges and on promoting each other’s regulatory frameworks, requirements and processes, as a basis for information-sharing.

  Swissmedic Announcement, 11 October 2016.

Use of medicines

Report on sales of veterinary antibiotics in Europe

European Union – The Sixth report on the sales of veterinary antibiotics in Europe highlights a slight downward trend, suggesting that actions taken by EU member states to fight antimicrobial resistance are making a difference.

A total of 28 countries reported data to the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) for the year 2014. While a considerable increase was noted in one European country due to an improvement in data collection systems, an overall decrease of 12% was found in 24 of the 25 countries that provided data for this four-year period. Other countries also changed their reporting systems or identified under-reporting, meaning that the findings should be interpreted with caution.

► EMA News, 14 October 2016.
  EMA. Sales of veterinary antimicrobial agents in 29 European countries in 2014: Sixth ESVAC report.

Indian FDC ban reversed

India – The Delhi High Court has stayed a government ban on 344 fixed-dose combination (FDC) medicines after more than six months of hearing more than 300 petitions filed by pharmaceutical companies. (1)

The ban, which affected analgesic and antibiotic combinations among others, had been announced in March 2016 in the interest of public health. (2)


Under discussion

European Union – The European Medicines Agency (EMA) has published a revised guideline on first-in-human clinical trials. The revision was based on a concept paper released for comment earlier in 2016 and took into account the lessons learnt from the tragic incident which occurred during a clinical trial in Rennes, France, in January 2016. The revised guideline is open for public consultation until 28 February 2017.


European Union – The European Commission (EC) is seeking views and feedback from stakeholders, to support the Commission in drafting its second report on the Paediatric Regulation after ten years of implementation. The consultation is open until 20 February 2017.

Approved

**Obeticholic acid for rare, chronic liver disease**

**Product name:** Ocaliva®

**Dosage form:** Tablets

**Class:** Bile acid preparation;

**ATC code:** A05AA04

**Approval:** EMA (orphan product; conditional approval)

**Use:** In combination with ursodeoxycholic acid (UDCA), treatment of primary biliary cholangitis (also known as primary biliary cirrhosis) in patients who cannot successfully be treated with UDCA alone.

**Benefits:** Ability to delay development of liver fibrosis, cirrhosis liver transplant and death through reduction of alkaline phosphatase and bilirubin levels in adults with primary biliary cholangitis. The efficacy remains to be formally demonstrated by means of post-authorization follow-up.

**Note:** In the past, the only option for these patients has been a liver transplant.

► EMA Press release, 14 October 2016.

**Insulin aspart for diabetes mellitus**

**Product name:** Fiasp®

**Dosage form:** Solution for injection

**Class:** Fast-acting insulin analogue;

**ATC code:** A10AB05

**Approval:** EMA

**Use:** Treatment of diabetes mellitus in adults

**Benefits:** Ability to control blood glucose.

**Note:** Fiasp® is an ultra-rapid-acting formulation of insulin aspart.

► EMA CHMP Summary of opinion, 10 November 2016.

**Insulin glargine/lixisenatide for diabetes mellitus**

**Product name:** Suliqua®

**Dosage form:** Solution for injection

**Class:** Fixed-ratio combination of insulin glargine, a basal insulin analogue, and lixisenatide, a glucagon-like peptide 1 (GLP-1) receptor agonist

**Approval:** EMA

**Use:** In combination with metformin, treatment of diabetes mellitus in adults when glycaemic control has not been provided by other treatments.

**Benefits:** Clinically relevant effect on glycaemic control in patients with type-2 diabetes when used with metformin.

► EMA CHMP Summary of opinion, 10 November 2016.

**Lonoctocog alfa for haemophilia A**

**Product name:** Afstyla®

**Dosage form:** Powder and solvent for solution for injection or infusion

**Class:** Single-chain recombinant human factor VIII product; **ATC code:** B02BD02

**Approval:** EMA CHMP recommendation

**Use:** Treatment and prophylaxis of bleeding in patients with haemophilia A.

**Benefits:** Ability to prevent and control bleeding when used on demand and when used for surgical procedures in adults and children with haemophilia A. Lonoctocog alfa has demonstrated a higher affinity for von Willebrand factor (VWF) than full-length recombinant factor VIII. VWF stabilises factor VIII and protects it from degradation.

► EMA Summary of opinion, 10 November 2016.

**Etelcalcetide for secondary hyperparathyroidism**

**Product name:** Parsabiv®

**Dosage form:** Solution for injection

**Class:** Synthetic peptide, calcimimetic agent

**ATC code:** H05BX04

**Approval:** EMA
Approved

Use: Treatment of secondary hyperparathyroidism in adults with chronic kidney disease on haemodialysis therapy.
Benefits: Ability to reduce abnormally elevated serum parathyroid hormone levels in patients with chronic kidney disease on haemodialysis therapy.
EMA Summary of opinion, 15 September 2016.

Tenofovir alafenamide for chronic hepatitis B
Product name: Vemlidy®
Dosage form: Film-coated tablets
Class: Nucleotide reverse transcriptase inhibitor; ATC code: J05AF13
Approval: EMA
Use: Treatment of chronic hepatitis B in adults and adolescents aged 12 years and older.
Benefits: Ability to achieve a sustained antiviral response in treatment-naive and treatment-experienced patients.
Safety information: Lower impact on renal safety and bone mineral density compared to tenofovir disoproxil.
EMA CHMP Summary of opinion, 10 November 2016.

Olaratumab for soft tissue sarcoma
Product name: Lartruvo®
Dosage form: Concentrate for solution for infusion
Class: Human IgG1 monoclonal antibody and antagonist of platelet derived growth factor receptor-α (PDGFR-α) expressed on tumour and stromal cells; ATC code: L01XC27
Approval: EMA (orphan product, accelerated assessment; conditional marketing authorization): FDA (orphan drug; fast track designation, priority review, breakthrough therapy, accelerated assessment)
Use: In combination with doxorubicin, treatment of adults with soft tissue sarcoma.
Benefits: Improved survival.
Safety information: Olaratumab has some serious risks including infusion-related reactions and embryo-foetal harm.
EMA Press release, 16 September 2016.
FDA News release, 19 October 2016.

Palbociclib for breast cancer
Product name: Ibrance®
Dosage form: Hard capsules
Class: Inhibitor of cyclin-dependent kinases (CDK) 4 and 6; ATC code: L01XE33
Approval: EMA
Use: In combination with other medicines, treatment of hormone receptor (HR)-positive and human epidermal growth factor receptor 2 (HER2)-negative locally advanced or metastatic breast cancer.
Benefits: Improved progression-free survival.
EMA Press release, 16 September 2016.

Eteplirsen for Duchenne muscular dystrophy
Product name: Exondys 51®
Dosage form: Injection for intravenous use
Class: Antisense oligonucleotide; ATC code: M09AX06 (temporary code)
Approval: FDA (orphan medicinal product, fast track designation; accelerated approval under a rare paediatric disease priority review voucher)
Use: Treatment of patients with Duchenne muscular dystrophy with a confirmed mutation of the dystrophin gene amenable to exon 51 skipping.
Benefits: Dystrophin increase in skeletal muscle (surrogate endpoint).
Notes: The FDA has required a study to assess whether the product improves motor function.
FDA News release, 19 September 2016.

Baricitinib for rheumatoid arthritis
Product name: Olumiant®
Dosage form: Tablets
Class: Selective and reversible inhibitor of Janus kinase (JAK) 1 and 2; ATC code: L04AA37

Approval: EMA

Use: Treatment of active rheumatoid arthritis in adults who cannot be treated with other disease-modifying anti-rheumatic drugs.

Benefits: Reduces the symptoms of rheumatoid arthritis

EMA Press release, 16 Dec 2016.

Naloxone nasal spray for opioid overdose

Product name: Narcan®

Dosage form: Nasal spray

Class: Antidote; ATC code: V03AB15

Approval: Health Canada (expedited review)

Use: Emergency treatment of opioid overdose (non-prescription use)

Notes: Since early 2016, naloxone is available without a prescription in Canada for emergency treatment of opioid overdose. A temporary import permit for a U.S. FDA-approved product was granted in July 2016.


Edotreotide for diagnosis of gastro-entero-pancreatic neuroendocrine tumours

Product name: SomaKit TOC®

Dosage form: Kit for radiopharmaceutical preparation

Class: Diagnostic radiopharmaceutical for tumour detection; ATC code: V09IX09

Approval: EMA (orphan product)

Use: After radiolabelling with gallium (68Ga) chloride solution, for Positron Emission Tomography (PET) imaging of somatostatin receptor overexpression in adult patients with well-differentiated gastro-entero-pancreatic neuroendocrine tumours.

Benefits: Ability to localize primary tumours and their metastases.

► EMA Summary of opinion, 13 October 2016.

Biosimilars

Insulin glargine

Product name: Lusduna®

Reference product: Lantus®

Approval: EMA

Use: Treatment of diabetes mellitus

► EMA/CHMP Summary of opinion, 10 November 2016.

Teriparatide

Product name: Movymia®

Reference product: Forsteo®

Approval: EMA

Use: Treatment of osteoporosis

► EMA/CHMP Summary of opinion, 10 November 2016.

Rituximab

Product name: Truxima®

Reference product: Mabthera®

Approval: EMA


► EMA Summary of opinion, 15 December 2016.

Adalimumab-atto

Product name: Amjevita®

Reference product: Adalimumab (Humira®)

Approval: FDA (biosimilar, not interchangeable with Humira®)

Use: Treatment of multiple inflammatory diseases in adult patients.
**Safety information:** Boxed Warning about an increased risk of serious infections, lymphoma and other malignancies, including some fatal ones, in children and adolescent patients treated with tumour necrosis factor blockers, including adalimumab products.


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**Extension of indications**

**Empagliflozin to reduce cardiovascular risk in diabetes**

**Product name:** Jardiance®

**Approval:** FDA

**Newly approved use:** To reduce the risk of cardiovascular death in adults with type 2 diabetes.

**Notes:** Empagliflozin is not intended for patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. It is contraindicated in patients with a history of serious hypersensitivity reactions to the medicine, severe renal impairment, end-stage renal disease, or those on dialysis.

► FDA News release, 2 December 2016.

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**Maravirocin for use in children**

**Product name:** Selzentry®

**Approval:** FDA

**Newly approved use:** For the treatment of CCR5-tropic human immunodeficiency virus type 1 (HIV 1) infection in patients 2 years of age and older weighing at least 10 kg.

**Note:** Maravirocin is not recommended in patients with dual/mixed- or CXCR4-tropic HIV-1.


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**Nivolumab for Hodgkins lymphoma**

**Product name:** Opdivo®

**Approval:** EMA

**Newly approved use:** Treatment of adult patients with relapsed or refractory classical Hodgkin lymphoma after autologous stem cell transplant and treatment with brentuximab vedotin.

► EMA/CHMP Summary of opinion, 13 October 2016.

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**Canakinumab for rare and serious auto-inflammatory diseases**

**Product name:** Ilaris®

**Approval:** FDA

**Newly approved use:** Treatment of Tumour Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS); Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD); and Familial Mediterranean Fever (FMF) in adults and children.

**Note:** Canakinumab was previously FDA-approved for another periodic fever syndrome called Cryopyrin-Associated Periodic Syndromes (CAPS) and for active systemic juvenile idiopathic arthritis.